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FORM PTO-1390
(REV 10-94)

U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE ATTORNEY'S DOCKET NUMBER

TRANSMITTAL LETTER TO THE UNITED STATES
DESIGNATED/ELECTED OFFICE (DO/EO/US)
CONCERNING A FILING UNDER 35 U.S.C. 371

P 2941 WO US

U.S. APPLICATION NO. (If known, enter 7 CFR 1.5)
08/981924

INTERNATIONAL APPLICATION NO.
PCT/DE 96/01296 ¹²⁶⁷ V, V

INTERNATIONAL FILING DATE
12 July 1996

PRIORITY DATE CLAIMED
12 July 1995

TITLE OF INVENTION

METHOD FOR DETERMINING THE EFFECTIVENESS AND TOLERANCE OF A XENOGENIC SUBSTANCE ADMINISTERED TO AN ORGANISM.

APPLICANT(S) FOR DO/EO/US

LAUK, Christiane

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. ☒ This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
 2. ☐ This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
 3. ☐ This express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1).
 4. ☒ A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.
 5. ☒ A copy of the International Application as filed (35 U.S.C. 371(c)(2))
 - a. ☐ is transmitted herewith (required only if not transmitted by the International Bureau).
 - b. ☒ has been transmitted by the International Bureau.
 - c. ☐ is not required, as the application was filed in the United States Receiving Office (RO/US)
 6. ☒ A translation of the International Application into English (35 U.S.C. 371(c)(2)).
 7. ☐ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))
 - a. ☐ are transmitted herewith (required only if not transmitted by the International Bureau).
 - b. ☐ have been transmitted by the International Bureau.
 - c. ☐ have not been made; however, the time limit for making such amendments has NOT expired.
 - d. ☒ have not been made and will not be made.
 8. ☐ A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
 9. ☒ An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).
 10. ☐ A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).
- Items 11. to 16. below concern document(s) or information included:
11. ☒ An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
 12. ☐ An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
 13. ☒ A **FIRST** preliminary amendment.
☐ A **SECOND** or **SUBSEQUENT** preliminary amendment.
 14. ☐ A substitute specification.
 15. ☐ A change of power of attorney and/or address letter.
 16. ☒ Other items or information:
 1. Return Postcard
 2. International Search Report
 3. title page of WO 97/03356
 4. FORM PCT/IB/308
 5. verified Small Entity Statement

17. ☒ The following fees are submitted:**BASIC NATIONAL FEE (37 CFR 1.492(a)(1)-(5)):**

Search Report has been prepared by the EPO or JPO..... \$930.00

International preliminary examination fee paid to USPTO (37 CFR 1.482)
..... \$720.00No international preliminary examination fee paid to USPTO (37 CFR 1.482)
but international search fee paid to USPTO (37 CFR 1.445(a)(2)).. \$790.00Neither international preliminary examination fee (37 CFR 1.482) nor
international search fee (37 CFR 1.445(a)(2)) paid to USPTO..... \$1070.00International preliminary examination fee paid to USPTO (37 CFR 1.482)
and all claims satisfied provisions of PCT Article 33(2)-(4)..... \$98.00**ENTER APPROPRIATE BASIC FEE AMOUNT =****CALCULATIONS** PTO USE ONLY

\$ 930.00

Surcharge of \$130.00 for furnishing the oath or declaration later than ☐ 20 ☐ 30
months from the earliest claimed priority date (37 CFR 1.492(e)).

| CLAIMS | NUMBER FILED | NUMBER EXTRA | RATE |
|---|--------------|--------------|--|
| Total claims | 8 -20 = | | X \$22.00 |
| Independent claims | 1 -3 = | | X \$82.00 |
| MULTIPLE DEPENDENT CLAIM(S) (if applicable) | | | + \$270.00 |
| TOTAL OF ABOVE CALCULATIONS | | | = |
| Reduction by 1/2 for filing by small entity, if applicable. Verified Small Entity Statement must also be filed (Note 37 CFR 1.9, 1.27, 1.28). | | | \$ 465.00 |
| SUBTOTAL | | | = |
| Processing fee of \$130.00 for furnishing the English translation later than <input type="checkbox"/> 20 <input type="checkbox"/> 30 months from the earliest claimed priority date (37 CFR 1.492(f)). | | | + |
| TOTAL NATIONAL FEE | | | = |
| Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). \$40.00 per property | | | + |
| TOTAL FEES ENCLOSED | | | = |
| | | | Amount to be: refunded \$ charged \$ |

a. ☐ A check in the amount of \$ _____ to cover the above fees is enclosed.b. ☐ Please charge my Deposit Account No. _____ in the amount of \$ _____ to cover the above fees.
A duplicate copy of this sheet is enclosed.c. ☐ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any
overpayment to Deposit Account No. _____. A duplicate copy of this sheet is enclosed.**NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.**Please send all correspondence
by FAX with AIRMAIL confirmation
to:

SEND ALL CORRESPONDENCE TO:

Paul J. Vincent
Schuster & Partner
Wiederholdstr. 10
D-70174 Stuttgart
Germany
Fax-Number: 0049/711/29 95 94

SIGNATURE:

Paul J. Vincent

NAME

37,461

REGISTRATION NUMBER

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Christiane LAUK) Examiner:
PCT Internat. Application No.: PCT/DE96/01269) Unknown
PCT Internat. Filing Date: 12 July 1996) Art Unit:
For: METHOD FOR DETERMINING THE EFFECTIVENESS Unknown
AND TOLERANCE OF A XENOGENIC SUBSTANCE
ADMINISTERED TO AN ORGANISM

Attorney Docket No.: P 2941 WO US

PRELIMINARY AMENDMENT

Commissioner of Patents and Trademarks
Washington, D.C. 20231

Dear Sir:

The Examiner is hereby requested to enter this preliminary amendment prior to the calculation of the filing fee as follows:

IN THE SPECIFICATION:

Please insert as a title between the title and the first paragraph --BACKGROUND OF THE INVENTION--.

On page 1, first paragraph, line 2, please replace "in accordance with the precharacterizing part of the main claim" with --having the following method steps: isolating the immune cells, introducing target cells, introducing a

substrate which changes its structure through the activity of cells, determining the base activity of the mixture of immune cells, target cells and the substrate using spectrometer analysis, adding the active substance, measuring the reaction activity of the mixture using spectrometer analysis, comparing the measurement results with the base activity and the reaction activity of the mixture and determining the strength of the reaction based on the comparison --.

On page 2, between the second and third paragraph, please replace "The Invention and its Advantages" with --SUMMARY OF THE INVENTION AND DESCRIPTION OF THE PREFERRED EMBODIMENT".

On page 2, third paragraph, first sentence, please replace "the method in accordance with the invention having the features in the characterizing portion of the main claim has the" with --in accordance with the invention, industrially applicable active substances in the form of xenogenic (not naturally occurring in the body) pharmaceutical products are utilized, only the immune cells of one human being or one single animal are utilized as immune cells, the reaction of the immune cells to the xenogenic pharmaceutical product is individually evaluated for the organism, the analysis determines the tolerance and/or effectiveness of the xenogenic pharmaceutical product for the organism, and, if necessary, the method is carried out either simultaneously or, in the event of undesirable effects, in series using differing xenogenic pharmaceutical products and/or pharmaceutical product mixtures to determine the optimal effectiveness and tolerance of possible alternative xenogenic pharmaceutical products available for selection. This has the--.

On page 5, following the sixth paragraph, please insert as a title --I CLAIM:--

IN THE CLAIMS:

Please delete claims 1 through 8 without prejudice and enter new claims 9 through 16 as indicated below:

9. A method for the determination of the activity of immune cells in dependence on a compound, comprising the following steps:

- a. isolating immune cells from an individual organism;
 - b. introducing target cells to said immune cells;
 - c. adding a substrate to said target and said immune cells, said substrate having a structure which changes via cell interactions;
 - d. determining a base activity of a mixture of said immune cells, said target cells, and said substrate using a spectrometer;
 - e. adding a first xenogenic pharmaceutical product to said mixture following step d;
 - f. measuring a reaction activity of said mixture following step e;
 - g. comparing said reaction activity to said base activity;
 - h. analyzing step g to determine at least one of a tolerance and effectiveness of said first product for said individual organism;
 - i. repeating steps a through g using a second xenogenic pharmaceutical product should step h produce undesirable effects; and
 - j. comparing said first and said second products, if step i is executed, to determine an optimal effectiveness and tolerance of possible alternative xenogenic pharmaceutical products available for selection for said individual organism.
10. The method of claim 9, wherein said xenogenic pharmaceutical product is selected from the group consisting of homoeopathic active substances, natural products of plant, animal and bacterial origin and mixtures of active substances.
 11. The method of claim 9, wherein said target cells comprise cancer cells.
 12. The method of claim 9, wherein said target cells comprise virus-infected cells.
 13. The method of claim 9, wherein said target cells ^{comprise} one of normal cells, allogenic cells, autogenic cells and xenogenic cells.
 14. The method of claim 9, wherein said substrate comprises a tetrazolium salt.

15. The method according to claim 14, wherein said tetrazolium salt comprises MTT (3-{4,5 dimethylthiazole-2-yl}-2,5-diphenyl tetrazolium bromide).
16. The method according to claim 14, wherein said tetrazolium salt comprises XTT (2,3-bis{2-methoxy-4-nitro-5-sulfophenyl}-5-({phenyl amino}carbonyl)-2H-tetrazolium hydroxide).

IN THE ABSTRACT:

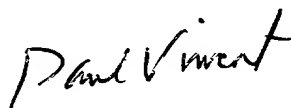
In line 2 of the abstract please replace "administered to an organism" with --on an individual organism without having to first administer the substance to the organism. The method allows for safe and reliable determination of the tolerance and effectiveness of xenogenic pharmaceutical products for a particular individual or animal.

REMARKS:

The amendments have been taken to modify the description, the claims and the abstract to United States practice. No new matter has been added.

THE EXAMINER IS RESPECTFULLY REQUESTED TO SEND ALL URGENT COMMUNICATIONS IN THIS CASE BY FAX. THANK YOU.

Respectfully submitted,



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Translation of PCT/DE 96/01269
filed: 12.07.1996

P 2941 WO US
V/Ni

METHOD FOR DETERMINING THE EFFECTIVENESS AND
TOLERANCE OF A XENOGENIC SUBSTANCE
ADMINISTERED TO AN ORGANISM

Prior Art

The invention concerns a method for the determination of the activity of immune cells in dependence on an active substance, in accordance with the precharacterizing part of the main claim.

Determination of the tolerance and effectiveness of pharmaceutical products such as homoeopathic, biological, natural and chemical compounds and compound mixtures for the patient being treated is decisive for successful therapy and treatment of a disease. The reaction of the patient to the pharmaceutical product is normally studied subsequent to administration.

A number of methods are known in the art for investigating the activity of immune cells with regard to various cells.

A conventional method (In: Naturwissenschaften 76, page 530 ff., 1989), the influence of the mistletoe plant (*Viscum album*) on the activity of immune cells is investigated with regard to cancer cells. Towards this end, cancer cells are marked with radioactive tritium and mixed with immune cells and mistletoe extract. The remaining amount of radioactivity of the mixture is determined after a certain period of time to provide information about the number of cancer cells destroyed by the immune cells. This method has the disadvantage that radioactive isotopes are necessary, that the precision depends on the number of cells investigated, and that the method is difficult and time consuming to carry out.

In another conventional investigation (In: Blood, Vol. 84, No. 10, November 1994, pages 3440 - 3346), the chemical sensitivity of B-lymphocytes is determined using the MTT-analysis procedure. Towards this end, the cytotoxicity of ambozile chloride (CLB) is compared with that of fludarabine, DNA topoisomerase 1 inhibitors, and other compounds. The B-lymphocytes thereby investigated come from patients suffering from B-CLL (chronic lymphocytic leukaemia). This investigation strives to develop a general prediction concerning the effectiveness of the compounds utilized and investigated for a group of patients suffering from a particular disease.

In the conventional method characterizing the instant invention (In: Cancer Immunology Immunotherapy, pages 393-398, 1992), the influence of intrinsic body compounds (Interferon γ , Tumor-Nectrosis-Factor- α) on cytostatica and cytotoxicity is investigated in human tissue cells (U 937). This method attempts to effect a general statement concerning the effectiveness of the compounds being investigated on certain types of tissue cells. The method concerns confirmation of a particular expected effectiveness.

The Invention and its Advantages

In contrast thereto, the method in accordance with the invention having the features in the characterizing portion of the main claim has the advantage that the tolerance and effectiveness of xenogenic pharmaceutical products on a human being or on individual animals can be determined. Towards this end, the scientifically developed conventional method is used in accordance with the invention for a new industrial application.

The goal of the conventional investigation characterizing the invention is to determine the effect of individual body compounds on immune cells and target cells, which could be infected cells, cancer cells or other cells. The primary aspect thereby is to develop a general statement concerning whether or not a particular compound has a certain

relationship to immune cells and the immune system of particular living organisms.

The new application in accordance with the invention of the modified procedure is not, in contrast thereto, intended to develop a general overall statement concerning the effect of certain individual body compounds. Rather, the individual tolerance and effectiveness of a pharmaceutical product not naturally occurring in the body is determined for a single patient. The results of the method provide information concerning the possible success of treatment. In this manner it is possible to determine, with the assistance of the method in accordance with the invention, whether and to what extent an individual patient reacts to a pharmaceutical product prior to administration of this pharmaceutical product. A plurality of similar compounds can also be tested to determine the one to which a particular patient best responds. For investigations of this type, blood is extracted from the patient from which the immune cells are isolated. These cells are then mixed with special target cells, e.g. with virus-infected cells, with cancer cells or with normal cells (autogenic, allogenic or xenogenic cells) and with the pharmaceutical product.

Without doubt, there has been a long felt need for a simple and economical method for determining and predicting whether or not and to what extent a patient would react to a pharmaceutical product and the chances for successful treatment prior to the administration of the pharmaceutical product. The method in accordance with the invention satisfies this need.

Although the method of prior art categorizing the instant invention has been known in the art since 1992 and although the activity analysis based on tetrazolium salt MTT for carrying out the method has been known in the art and used for similar purposes in scientific investigations since at least 1988 (see Cancer Research 48; 589-601, 1988), this conventional method has only been used for analytic scientific applications up to the point of time of the instant invention.

An additional advantage of the method in accordance with the invention is that extremely expensive and/or risky pharmaceutical products having side-effects can be tested for effectiveness and tolerance to patients prior to administration thereof. Precisely such compounds often require proof of effectiveness of the pharmaceutical product for insurance purposes in order to recover costs for the pharmaceutical product.

An additional advantage of the invention is that the method can be carried out simultaneously with or, in the event of undesirable effects, in series using different xenogenic pharmaceutical products and/or pharmaceutical product mixtures. Proceeding in this manner has the advantage that the optimal effectiveness and tolerance of possible alternative xenogenic pharmaceutical products from which a selection is to be made can be determined.

In accordance with an advantageous embodiment of the invention, homeopathic compounds and compound mixtures are utilized as the xenogenic pharmaceutical product. In particular, for homeopathy, in which very low doses of compounds which, in healthy individuals at higher doses create a similar disease pattern, are administered to treat diseases, it is reasonable to determine the effectiveness and tolerance of the compound for the patient prior to administering same. In addition, the method has the invention that the effectiveness and tolerance can be tested at doses higher than those used on the patient.

In accordance with an additional advantageous embodiment of the invention, cancer cells are utilized as target cells. In this manner, the effect of a pharmaceutical product can be investigated, in particular with cancer patients.

In accordance with an additional advantageous embodiment of the invention, virus-infected cells are utilized as target cells.

In accordance with an additional advantageous embodiment of the invention, normal cells (allogenic, autogenic or xenogenic cells) are utilized as target cells.

In accordance with an additional advantageous embodiment of the invention, tetrazolium salts are utilized as coloring agents.

In accordance with an additional advantageous embodiment of the invention, the tetrazolium salt MTT is utilized as the substrate. This substrate is a yellow tetrazolium salt. The dehydrogenase in the active mitochondria of living cells converts this yellow salt into a blue formazan crystal. This transformation only occurs in living cells and has differing strength in immune cells and target cells. With the assistance of a spectrometer, the color of the sample can be investigated which, in turn, provides information concerning the number of target cells which have been destroyed by the immune cells.

In accordance with an additional advantageous embodiment of the invention, the tetrazolium salt XTT is utilized as the substrate. This substrate provides more precise measurement results for specific applications.

Further advantages and advantageous embodiments of the invention can be extracted from the claims.

All of the features represented in the description and the subsequent claims can be significant to the invention individually or collectively in arbitrary combination.

Claims:

1. Method for the determination of the activity of immune cells in dependence on a compound, having the following method steps:
 - isolating the immune cells,
 - introducing target cells,
 - introducing a substrate which changes its structure through the activity of cells,
 - determining the base activity of the mixture of immune cells, target cells and the substrate using spectrometer analysis,
 - adding the active substance,
 - measuring the reaction activity of the mixture using spectrometer analysis,
 - comparing the measurement results with the base activity and the reaction activity of the mixture,
 - determining the strength of the reaction based on the comparison,
 characterized in that
 - industrially applicable active substances in the form of xenogenic (not naturally occurring in the body) pharmaceutical products are utilized,
 - only the immune cells of one human being or one single animal are utilized as immune cells,
 - the reaction of the immune cells to the xenogenic pharmaceutical product is individually evaluated for the organism,
 - the analysis determines the tolerance and/or effectiveness of the xenogenic pharmaceutical product for the organism, and,
 - if necessary, the method is carried out either simultaneously or, in the event of undesirable effects, in series using differing xenogenic pharmaceutical products and/or pharmaceutical product mixtures to determine the optimal effectiveness and tolerance of possible alternative xenogenic pharmaceutical products available for selection.

2. Method according to claim 1, characterized in that homeopathic active substances, natural products of plant, animal and bacterial origin or mixtures of active substances are utilized as the xenogenic pharmaceutical product.
3. Method according to claim 1, characterized in that cancer cells are utilized as target cells.
4. Method according to claim 1, characterized in that virus-infected cells are utilized as target cells.
5. Method according to claim 1, characterized in that normal cells (allogenic, autogenic or xenogenic cells) are utilized as target cells.
6. Method according to any one of the preceding claims, characterized in that a tetrazolium salt is utilized as the substrate.
7. Method according to claim 6, characterized in that the tetrazolium salt MTT (3-{4,5 dimethylthiazole-2-yl}-2,5-diphenyl tetrazolium bromide) is utilized.
8. Method according to claim 6, characterized in that the tetrazolium salt XTT (2,3-bis{2-methoxy-4-nitro-5-sulfophenyl}-5-({phenyl amino}carbonyl)-2H-tetrazolium hydroxide) is utilized.

A method is proposed for determining the effectiveness and tolerance of a xenogenic substance administered to an organism.

Applicant or Patentee: LAUK, Christiane
Serial or Patent No.: PCT/DE 96/01269
Filed or Issued: 12 July 1996
For: METHOD FOR DETERMINING THE EFFECTIVENESS AND
TOLERANCE OF A XENOGENIC SUBSTANCE ADMINISTERED TO AN ORGANISM
Attorney's Docket No.: P 2941 WO US

VERIFIED STATEMENT (DECLARATION) CLAIMING SMALL ENTITY STATUS
(37 CFR 1.9(f) and 1.27(c)) - SMALL BUSINESS CONCERN

I hereby declare that I am
(X) an Individual
() the owner of the small business concern identified below:
() an official of the small business concern empowered to act on
behalf of the concern identified below:

Name of Concern Dr. Christiane Lauk
Address of Concern Unterer Bühlweg 1, 71159 Mötzingen, Germany

I hereby declare that the above identified small business concern qualifies as a small business concern as defined in 13 CFR 121.3-18, and reproduced in 37 CFR 1.9(d), for purposes of paying reduced fees under section 41(a) and (b) of Title 35, United States Code, in that the number of employees of the concern, including those of its affiliates, does not exceed 500 persons. For purposes of this statement, (1) the number of employees of the business concern is the average over the previous fiscal year of the concern of the persons employed on a full-time, part-time or temporary basis during each of the pay periods of the fiscal year, and (2) concerns are affiliates of each other when either, directly or indirectly, one concern controls or has the power to control the other, or a third party or parties controls or has the power to control both.

I hereby declare that rights under contract or law have been conveyed to and remain with the small business concern identified above with regard to the invention, entitled METHOD FOR DETERMINING THE EFFECTIVENESS AND TOLERANCE OF A XENOGENIC SUBSTANCE ADMINISTERED TO AN ORGANISM by inventor(s)

Lauk, Christiane
described in

() the specification filed herewith
(X) application Serial No. , filed PCT/DE96/01269 -12 July 1996
() Patent No. , issued .

If the rights held by the above identified small business concern are not exclusive, each individual, concern or organization having rights to the invention is listed below* and no rights to the invention are held by any person, other than the inventor, who could not qualify as a small business concern under 37 CFR 1.9(d) or by any concern which would not qualify as a small business concern under 37 CFR 1.9(d) or a nonprofit organization under 37 CFR 1.9(e). *NOTE: Separate verified statements are required from each named person, concern or

Verified Statement (Declaration) Claiming Small Entity Status
(37 CFR 1.9(f) and 1.27(c)) - Small Business Concern - page 2

organization having rights to the invention averring to their status as small entities. (37 CFR 1.27)

Full Name Dr. Christiane Lauk

Address Unterer Bühlweg 1, 71159 Mötzingen, Germany

☒ Individual ☐ Small Business Concern ☐ Nonprofit Organization

Full Name _____

Address _____

☐ Individual ☐ Small Business Concern ☐ Nonprofit Organization

Full Name _____

Address _____

☐ Individual ☐ Small Business Concern ☐ Nonprofit Organization

I acknowledge the duty to file, in this application or patent, notification of any change in status resulting in loss of entitlement to small entity status prior to paying, or at the time of paying, the earliest of the issue fee or any maintenance fee due after the date on which status as a small entity is no longer appropriate. (37 CFR 1.28(b))

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application, any patent issuing thereon, or any patent to which this verified statement is directed.

Name of Person Signing Dr. Christiane Lauk

Title of Person Other than Owner _____

Address of Person Signing Unterer Bühlweg 1, 71159 Mötzingen
Germany

Signature

Christiane Lauk

Date _____

COMBINED DECLARATION FOR PATENT APPLICATION AND POWER OF ATTORNEY

(Includes Reference to PCT International Applications)

ATTORNEY DOCKET NUMBER

P 2941 WO US

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name,

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled

METHOD FOR DETERMINING THE EFFECTIVENESS AND TOLERANCE OF A

XENOGENIC SUBSTANCE ADMINISTERED TO AN ORGANISM

the specification of which (check only one item below):

☐ is attached hereto.

☐ was filed as United States application

Serial No. _____

on _____,

and was amended

on _____ (if applicable)

☒ was filed as PCT international application

Number PCT/DE 96/01269

on 12 July 1996,

and was amended under PCT Article 19

on _____ (if applicable)

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is known to me or other person(s) involved in the preparation or prosecution of this application to be material to the examination of this application and to patentability as defined in Title 37, Code of Federal Regulations, §1.56.

I hereby authorize the U.S. attorney or agent named herein to accept and follow instructions from _____

as to any action taken in the Patent and Trademark Office regarding this application without direct communication between the U.S. attorney or agent and the undersigned. In the event of a change in the persons from whom instructions may be taken, the U.S. attorney or agent named herein will be so notified by the undersigned.

I hereby claim foreign priority benefits under Title 35, United States Code, §119 of any foreign application(s) for patent or inventor's certificate or of any PCT international application(s) designating at least one country other than the United States of America listed below and have also identified below any foreign application(s) for patent or inventor's certificate or any PCT international application(s) designating at least one country other than the United States of America filed by me on the same subject matter having a filing date before that of the application(s) of which priority is claimed:

PRIOR FOREIGN/PCT APPLICATION(S) AND ANY PRIORITY CLAIMS UNDER 35 U.S.C. 119

| COUNTRY (if PCT, indicate "PCT") | APPLICATION NUMBER | DATE OF FILING (day, month, year) | PRIORITY CLAIMED UNDER 35 USC 119 | |
|-------------------------------------|--------------------|--------------------------------------|---|-----------------------------|
| DE (Germany) | 195 25 133.4 | 12 July 1995 | <input checked="" type="checkbox"/> YES | <input type="checkbox"/> NO |
| | | | <input type="checkbox"/> YES | <input type="checkbox"/> NO |
| | | | <input type="checkbox"/> YES | <input type="checkbox"/> NO |
| | | | <input type="checkbox"/> YES | <input type="checkbox"/> NO |
| | | | <input type="checkbox"/> YES | <input type="checkbox"/> NO |

Combined Declaration For Patent Application and Power of Attorney (Continued)

(Includes Reference to PCT International Applications)

ATTORNEY DOCKET

P 2941 WO

I hereby claim the benefit under Title 35, United States Code, §120 of any United States application(s) or PCT international application(s) designating the United States of America that is/are listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in that/those prior application(s) in the manner provided by the first paragraph of Title 35, United States Code, §112, I acknowledge the duty to disclose material information as defined in Title 37, Code of Federal Regulations, §1.56(a) which occurred between the filing date of the prior application(s) and the national or PCT international filing date of this application:

PRIOR U.S. APPLICATIONS OR PCT INTERNATIONAL APPLICATIONS DESIGNATING THE U.S. BENEFIT UNDER 35 U.S.C. 120

U.S. APPLICATIONS

STATUS (Check one)

U.S. APPLICATION NUMBER

U.S. FILING DATE

PATENTED

PENDING

ABANDONED

PCT APPLICATIONS DESIGNATING THE U.S.

PCT APPLICATION NUMBER

PCT FILING DATE

U.S. SERIAL NUMBERS
ASSIGNED (if any)

POWER OF ATTORNEY: As a named inventor, I hereby appoint the following attorney(s) and/or agent(s) to prosecute this application and transact all business in the Patent and Trademark Office connected therewith. (List name and registration number)

Paul J. Vincent Reg. No. 37,461

Send Correspondence to:

Schuster & Partner
Wiederholdstr. 10
70174 Stuttgart
Germany

Direct Telephone Calls to:

Country Code: 49
City Code: 711
Number: 29 95 91

| | | | | |
|-----|-------------------------|-------------|--------------------------|------------------------|
| 201 | FULL NAME OF INVENTOR | FAMILY NAME | FIRST GIVEN NAME | SECOND GIVEN NAME |
| | RESIDENCE & CITIZENSHIP | CITY | STATE OR FOREIGN COUNTRY | COUNTRY OF CITIZENSHIP |
| | POST OFFICE ADDRESS | CITY | STATE & ZIP CODE/COUNTRY | |
| 202 | FULL NAME OF INVENTOR | FAMILY NAME | FIRST GIVEN NAME | SECOND GIVEN NAME |
| | RESIDENCE & CITIZENSHIP | CITY | STATE OR FOREIGN COUNTRY | COUNTRY OF CITIZENSHIP |
| | POST OFFICE ADDRESS | CITY | STATE & ZIP CODE/COUNTRY | |
| 203 | FULL NAME OF INVENTOR | FAMILY NAME | FIRST GIVEN NAME | SECOND GIVEN NAME |
| | RESIDENCE & CITIZENSHIP | CITY | STATE OR FOREIGN COUNTRY | COUNTRY OF CITIZENSHIP |
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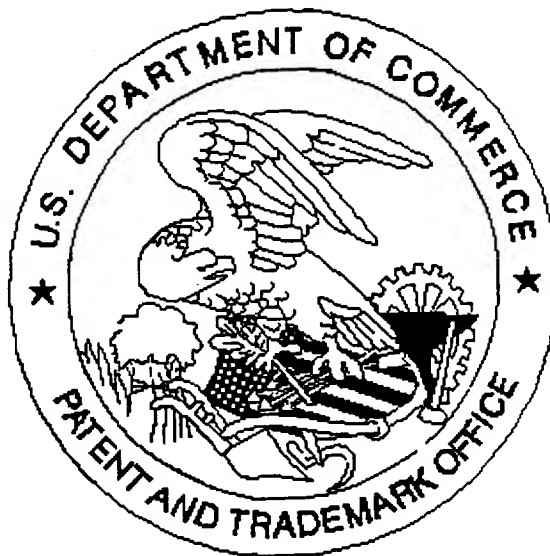
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